

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Hitoshi FUKUSHIMA et al. Art Unit : Unknown
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Title : MANUFACTURE OF A MICROSENSOR DEVICE AND A METHOD FOR
EVALUATING THE FUNCTION OF A LIQUID BY THE USE THEREOF

Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the specification:

Please replace the paragraph beginning at page 1, line 12 with the following rewritten paragraph:

A biosensor system as a means to monitor a biological function instantaneously has been intensively studied and developed for practical applications heretofore. The basic composition of a biosensor consists of a section for detecting a biological substance and a section for transducing a signal. A biological substance is complexed with the recognizing component of the biosensor, and ensures an ability to detect a bio-molecule, while the signal transducing section transduces a change obtained through the detection of a biological substance into an electric signal. There are many kinds of biological substances which can be detected on the basis of their molecular properties, and they include enzymes, antibodies, binding proteins, lectin, receptors, etc. Examples of biological substances include those that have a molecule recognizing ability and/or catalyzing function. They include enzymes, complex enzyme systems, intracellular organelles, microorganisms, animal cells, plant cells, etc. The catalytic activity of these substances depends on the structure characteristic with enzymes, and can be approximated, in its essence, by the kinetic equation by Michaelis and Menten. Other examples include substances that have a molecule recognizing function, and which forms a stable complex through a biological affinity. They include antibodies, lectin, binding proteins, receptors, etc. The basic designing of a bio-sensor proceeds with attention paid to the above properties. With the recent development of biotechnology, the range of biological substances available for the biosensor has been widened, and thus thermo-resistive enzymes, monoclonal

antibodies or the like have come have to be available. To convert the data obtained through molecule recognition into electric signals, physical parameter converting elements such as electrochemical reactions, and an FET, thermistor, piezoelectric element, surface elastic wave element, photodiode, etc. have been utilized.

Please replace the paragraph beginning at page 2, line 14 with the following rewritten paragraph:

However, the above-described conventional biosensor devices have technical problems as described below. Firstly, the method for producing a thin film for molecular recognition includes methods based on photoresistance, electrochemical polymerization, manufacture of an LB film, etc. The method based on photoresistance consists of forming a photoresistant film on the entire surface of an ISFET (ion sensitive field effect transistor), exposing only gate parts by lithography, and forming a highly affinitive molecule recognizing film (organic film or biomolecular film) on a gate insulating film. Then, the photoresistant layer is peeled off to leave the molecule recognizing film bonded to gate parts, which serves as a sensor. With this method, however, it is difficult to neatly prepare minute dot electrodes on the molecule recognizing film, and thus an incompletely finished edge of dots results. A reduced yield occurs. Further, waste of materials occurs as a result of lithography. Namely, 99% of photo-setting resin is discarded without being incorporated into actual products, that is, the method causes a wasteful consumption of resources on earth, and contamination of natural environments. This is a big problem. LB technique (Langmuir-Blodgett's technique) is a method whereby a mono-molecular film is formed on the surface of water, and the film is transferred onto the surface of a solid substrate, and for the method to be effective, it is necessary for the mono-molecular layer to have a structure comprising hydrophobic and hydrophilic sections in a balanced state. This method, however, is problematic in that the quality of LB film produced thereby is unsatisfactory in reliability: The film has immeasurable flaws or pores thereupon, and does not allow the formation of an uniform molecular film. Accordingly, with the product manufactured by this method, it is difficult to distinguish a change detected by a molecule recognizing film formed on an electrode from a local change of the electrode.

Please replace the paragraph beginning at page 4, line 1 with the following rewritten paragraph:

Namely, one object of this invention is to provide a method for forming, distinct from conventional methods, a molecule recognizing film, uniform and high in quality on a sensor electrode efficiently and in a short time. Further, another object of this invention is to provide a method for forming a plurality of minute sensor electrode dots by said new method for preparing a molecule recognizing film, and for accurately applying a great number of biological samples to be evaluated onto said plural minute sensor electrode dots in a short time and efficiently.

Please replace the paragraph beginning at page 4, line 11 with the following rewritten paragraph:

SUMMARY

According to one aspect of this invention, with a sensor device comprising organic thin films formed on an arbitrarily chosen electrode board circuit and electrodes, and a transducing element to transduce information obtained by the organic thin films into electric signals, provided is a method for producing the sensor device wherein a solution of a material of the thin film is accurately printed via an ink-jet nozzle as micro-dots onto the required surface of microelectrodes so that the organic thin films are formed on the electrodes, thereby realizing highly dense microelectrodes.

Please replace the paragraph beginning at page 4, line 21 with the following rewritten paragraph:

According to another aspect of this invention, provided is the sensor device as described in claim 1 wherein the solution of a material of the thin film comprises an electro-conductive polymer dissolved in a solvent.

Please replace the paragraph beginning at page 4, line 24 with the following rewritten paragraph:

According to another aspect of this invention, provided is the sensor device as described in claim 1 wherein the solution of a material of the thin film as described in claim 1 comprises a solution of a silicone-based surface modifying agent, or a mixture thereof with a solvent.

Please replace the paragraph beginning at page 5, line 1 with the following rewritten paragraph:

According to another aspect of this invention, provided is the sensor device as described in claim 1 wherein the solution of a material of the thin film as described in claim 1 comprises a mixture resulting from dissolution of a thiol compound in a solvent, and gold thin films are formed on the surface of the electrodes.

Please replace the paragraph beginning at page 5, line 6 with the following rewritten paragraph:

According to another aspect of this invention, with said sensor device, provided is a method for evaluating a trace amount of liquid wherein a solution of a sample substance to be sensed is ejected into air as micro-dots via an ink-jet nozzle to fall on the surface of organic thin films of microelectrodes so that the substance is submitted to evaluation.

Please replace the paragraph beginning at page 5, line 11 with the following rewritten paragraph:

According to another aspect of this invention, with said sensor device, provided is a method for evaluating a trace amount of liquid wherein the solution or liquid substance to be sensed and ejected into air as micro-dots via the ink-jet nozzle as described in claim 5 comprises a protein,

DNA, antibody, receptor, lectin, a bio-molecule from an animal or plant cell, or a physiologically active substance, or an aqueous solution thereof.

Please replace the paragraph beginning at page 5, line 18 with the following rewritten paragraph:

According to another aspect of this invention, provided are the sensor device and the method for evaluating the function of a liquid wherein the electrode or electric circuit is formed on a plastic substrate.

Please replace the paragraph beginning at page 5, line 21 with the following rewritten paragraph:

According to another aspect of this invention, provided are the sensor device and the method for evaluating the function of a liquid based on the use of the sensor device wherein the electric circuit is composed of poly-silicon thin film transistors.

Please replace the paragraph beginning at page 6, line 1 with the following rewritten paragraph:

Fig. 1 illustrates how minute electro-conductive polymer electrodes are formed by the method of this invention based on the use of an ink-jet.

Please replace the paragraph beginning at page 6, line 4 with the following rewritten paragraph:

Fig. 2 illustrates how a functional solution sample is analyzed based on the use of an ink-jet.

Please replace the paragraph beginning at page 6, line 7 with the following rewritten paragraph:

Fig. 3 illustrates how a plurality of functional solution samples are analyzed in a short period on electro-conductive polymer electrodes based on the use of an ink-jet.

Please replace the paragraph beginning at page 6, line 11 with the following rewritten paragraph:

Fig. 4 illustrates the principle underlying the assay method of the microsensor device.

Please replace the paragraph beginning at page 6, line 13 with the following rewritten paragraph:

Fig. 5 shows an electronic circuit to collect data for analysis using a microsensor device.

Please replace the paragraph beginning at page 6, line 15 with the following rewritten paragraph:

Fig. 6 shows an electronic circuit to collect data for analysis using another microsensor device of this invention.

Please replace the paragraph beginning at page 6, line 17 with the following rewritten paragraph:

Fig. 7 illustrates how sensor thin membranes having various detection activities are formed on the microelectrodes of a microsensor device.

Please replace the paragraph beginning at page 6, line 22 with the following rewritten paragraph:

One embodiment of the present invention will be described below with reference to attached figures.

Please replace the paragraph beginning at page 6, line 24 with the following rewritten paragraph:

Figs. 1, 2, 3, 4, 5 and 6 show parts of interest to illustrate the structure of a sensor device embodying the present invention. Fig.1 gives a schematic view of an ink-jet head: 10 stands for an inkjet head; 11 for a head nozzle for ejecting ink droplets; 12 for an electro-conductive polymer applied on the surface of an electrode; 13 for TFT microelectrodes; and 14 for suspended ink droplets ejected via the ink-jet nozzle. The ink-jet head is driven by a piezo-electric element, activating mode, whereby, when an electric signal is delivered from a driving circuit to the piezo-electric element, the piezo-electric element is deformed; a liquid within is pushed out by the deforming pressure; and the liquid is ejected via the nozzle.

Please replace the paragraph beginning at page 10, line 9 with the following rewritten paragraph:

Then, the assay dependent on the use of a sensor device array produced in the manner as described above will be described. Fig. 4 gives a simple block diagram of a circuit responsible for the assay dependent on the use of a resistor sensor array. Principal functions depicted in the figure are roughly presented by a resistor sensor multiplex section, signal processing circuit section and pattern recognizing section. Namely, the function depicted in this figure includes picking up signal from a single channel out of the multi-channel resistors, and processing and recognizing it. Accordingly, it is firstly important to accurately detect a change in impedance.

Please replace the paragraph beginning at page 10, line 20 with the following rewritten paragraph:

The simplest and most accurate way of determining a resistance includes various bridge methods, but these methods are not suitable for measuring a change in resistance. An alternative method includes a resistance to frequency conversion. This method, however, is disadvantageous in that it is accompanied by noise, and requires a rather longtime for measurement. As one general method for detecting a change in resistance, a circuit working on a voltage mode as shown in Fig. 5 has been known. In this circuit, a specific type of resistance sensor is chosen; a constant current is applied to it; and the voltage across the sensor is monitored. Then, as the voltage varies in proportion to the resistance, it is possible to detect a change in resistance by following a change in voltage. To determine changes in resistance it is advisable to subtract the voltage given as a base to the sensor by means of a differential amplifier, and then to amplify the differential signal with a high-gain amplifier. The sensitivity of the circuit depicted in Fig. 5 is proportional to the gain of amplifier, and is given by the following equation:

$$V_o = A (I_s R_s - V_{off}),$$

$$\text{where } (\delta V_o / \delta R_s) = A I_s.$$

Please replace the paragraph beginning at page 11, line 11 with the following rewritten paragraph:

An alternative method by which to detect a change in resistance includes a method working on a current mode. Fig. 6 gives a circuit diagram of the method. In this figure, a constant voltage is applied to a resistor sensor chosen for this purpose. To measure a change in resistance, a constant current supplied from a source is applied to the sensor as an offset current; differences in current are removed as a signal; and the signal is amplified. The sensitivity of the circuit is proportional to the current gain of amplifier and to the resistance of sensor.

$$I_0 = A (I_{off} - V_s / R_s)$$

where

$$(\delta I_{0s}/\delta R_s)=A_s/R_s^2=AI_s/R_s$$

This type of current detection method commands a higher degree of freedom than does the voltage detection method, and thus simplifies the subsequent processing of signals.

Please replace the paragraph beginning at page 11, line 26 with the following rewritten paragraph:

The above-described semiconductor circuits are usually constituted of field effect transistors (FET) arranged on a monocrystal silicon substrate. However, because in recent years the function of thin film transistors (TFT) formed on a polycrystal silicon (P-Si) film has made a notable progress, it becomes possible to prepare this type of circuit using polycrystal Si thin film transistors (P-Si TFT). The P-Si TFT has advanced so much that its function is essentially equal to that of monocrystal FET. Further, introduction of the method enabling the manufacture of polysilicon at a low temperature allows the use of a spacious glass substrate. This brings about a great cost-reduction and a method that is suitable for the production of sensor devices like the one described herein.

Please replace the paragraph beginning at page 13, line 3 with the following rewritten paragraph:

Several sensor arrays formed of field effect TFTs could be used for the simultaneous identification, classification and quantification of odours or other molecules. These sensors could be used in conjunction with other sensors to detect chemicals. The TFT sensors could be integrated onto a single device. Different electro-conductive polymers are placed upon the gates of the TFT sensors using ink-jet technology. In another modification the array of TFTs could be constructed in a pattern to produce a two-dimensional map of the odour response. The output from each TFT would then resemble the output from a pixel of a CCD camera. Different conducting polymers could be deposited onto different regions of the array to produce a device which was specific to a

group or class of chemicals, e. g. aromatics. When the molecules bind to or react with the polymer a two-dimensional map corresponding to the particular odours will appear.

Please replace the paragraph beginning at page 14, line 20 with the following rewritten paragraph:

Or, it is possible to plate a gold thin film onto the surface of a microelectrode such that a thiol molecule and gold interact with each other to form a self-organizing agglutination, which results in the formation of a functional, monolayer film. The functional group projecting from the surface of thiol monolayer which has been generated as a result of self-assembly on the gold thin film plated on the microelectrode has a function to selectively recognize a specific bio-molecule or a volatile molecule. For example, as the functional group projecting from the thiol molecule, a biotin derivative may be used. A biotin molecule has a strong binding activity towards a specific binding site of avidin or streptavidin, and its binding constant is about 10^{15} . This is practically the same as that encountered in a covalent bond. To this biotin molecule film is transferred, for example, a solution of avidin-ferritin binding protein via an inkjet nozzle. Then, avidin and biotin are selectively adsorbed; and the ferritin protein molecule is stabilized on the electrode. The thus selectively adsorbed molecule causes a change in refractive index of the entire molecular film, and that change is captured as a change in dielectric constant of the adsorbing molecular film. Namely, it is possible to convert the microelectrode into a polarized thin film (capacitor), which serves as a sensor.

Please replace the paragraph beginning at page 15, line 14 with the following rewritten paragraph

ADVANTAGES

According to this invention, provided is a method by which, in contrast with conventional ones, a molecule recognizing film is efficiently and in a short period formed on a microsensor in a uniform and high quality manner. Further, according to this invention, provided is a method by which to accurately introduce a vast number of biological samples to be evaluated in a short period

and efficiently to plural, minute sensor electrode dots which have been prepared according to said method for the formation of a molecule recognizing film.

In the Abstract

Please replace the original abstract with the following abstract:

In order to form organic thin films on electrodes, a solution of a material for the organic thin film is accurately printed via an ink-jet onto the surface of microelectrodes as required, thereby producing a high density array of microelectrodes. Further, a solution of a sample substance or a liquid substance to be sensed is ejected into air via an ink-jet nozzle to fall to the surface of organic thin membranes on the microelectrodes so that the sample can be evaluated.

In the claims:

Please cancel claims 1-10 and 18-26.

Please amend claim 11 as follows:

--11. A sensor device comprising:

a circuit having electrodes, wherein at least one of the electrodes comprises an organic thin film formed by printing a solution of a thin film material onto a surface of the electrode; and

a transducing element capable of transducing information recognized by the organic thin film into electric signals.--

Please add claims 27-32 as follows:

--27. The sensor device of claim 11 wherein the organic thin film formed on the electrode comprises a film formed from at least one dot.--

--28. The sensor device of claim 27 wherein the dot comprises a micro-dot.--

--29. The sensor device of claim 27 wherein the dot comprises a dot-shaped area.--

--30. The sensor device of claim 11 wherein the organic thin film formed on the electrode comprises a film formed from multiple dots.--

--31. The sensor device of claim 30 wherein the dot comprises a micro-dot.--

--32. The sensor device of claim 30 wherein the dot comprises a dot-shaped area.--

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Applicant : Hitoshi FUKUSHIMA et al.
Serial No. : Not assigned yet
Filed : June 1, 2001
Page : 13

Attorney's Docket No.: 04783-026002 / S279-N03-
P072-US/em

REMARKS

Claims 11-17 and 27-32 are pending in this application with claim 11 being independent. Claims 1-10 and 18-26 have been cancelled and claim 11 has been amended. Claims 27-32 have been added. The above amendments have been made to place the application in better condition for initial examination. No new matter has been added.

The examiner is invited to contact the undersigned with any questions at the number set forth below. Attached is a marked-up version of the changes being made by the current amendment.

Please apply any charges of credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: June 1, 2001

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Version with markings to show changes made

In the specification:

The paragraph beginning at page 1, line 12 has been amended as follows:

A biosensor system as a means to monitor a biological function instantaneously has been intensively studied and developed for practical applications heretofore. The basic composition of a biosensor consists of a section for detecting a biological substance and a section for transducing a signal. A biological substance is complexed with the recognizing component of the biosensor, and ensures an ability to detect a bio-molecule, while the signal transducing section transduces a change obtained through the detection of a biological substance into an electric signal. There are many kinds of biological substances which can be detected on the basis of their molecular properties, and they include enzymes, antibodies, binding proteins, lectin, receptors, etc. **[What comes first includes]** Examples of biological substances include those that have a molecule recognizing ability and/or catalyzing function. They include enzymes, complex enzyme systems, intracellular organelles, microorganisms, animal cells, plant cells, etc. The catalytic activity of these substances **[depend]** depends on the structure characteristic with enzymes, and can be approximated, in its essence, by the kinetic equation by Michaelis and Menten. **[What comes next includes]** Other examples include substances that have a molecule recognizing function, and which **[forms]** form a stable complex through a biological affinity. They include antibodies, lectin, binding proteins, receptors, etc. The basic designing of a bio-sensor proceeds with **[an]** attention paid to the above properties. With the recent development of biotechnology, the range of biological substances available for the biosensor has been widened, and thus thermo-resistive enzymes, monoclonal antibodies or the like have come to be available. To convert the data obtained through molecule recognition into electric signals, physical parameter converting elements such as electrochemical reactions, and an FET, thermistor, piezoelectric element, surface elastic wave element, photodiode, etc. have been utilized.

The paragraph beginning at page 2, line 14 has been amended as follows:

However, the above-described conventional biosensor devices have technical problems as described below. Firstly, the method for producing a thin film for molecular recognition includes methods based on photoresistance, electrochemical polymerization, manufacture of an LB film, etc. The method based on photoresistance consists of forming a photoresistant film on the entire surface of an ISFET (ion sensitive field effect transistor), exposing only gate parts by lithography, and forming a highly affinitive molecule recognizing film (organic film or biomolecular film) on a gate insulating film. Then, the photoresistant layer is peeled off to leave the molecule recognizing film bonded to gate parts, which serves as a sensor. With this method, however, it is difficult to neatly prepare minute dot electrodes on the molecule recognizing film, and thus **[the]** an incompletely finished edge of dots results. A reduced yield occurs. Further, waste of materials occurs as a result of lithography. Namely, 99% of photo-setting resin is discarded without being incorporated into actual products, that is, the method causes a wasteful consumption of resources on earth, and contamination of natural environments. This is a big problem. LB technique (Langmuir-Blodgett's technique) is a method whereby a mono-molecular film is formed on the surface of water, and the film is transferred onto the surface of a solid substrate, and for the method to be effective, it is necessary for the mono-molecular layer to have a structure comprising hydrophobic and hydrophilic sections in a balanced state. This method, however, is problematic in that the quality of LB film produced thereby is unsatisfactory in reliability: the film has immeasurable flaws or pores thereupon, and does not allow the formation of an uniform molecular film. Accordingly, with the product manufactured by this method, it is difficult to distinguish a change detected by a molecule recognizing film formed on an electrode from a local change of the electrode.

The paragraph beginning at page 4, line 1 has been amended as follows:

Namely, **[the first]** one object of this invention is to provide a method for forming, distinct from conventional methods, a molecule recognizing film, uniform and high in quality on a sensor electrode efficiently and in a short time. Further, **[the second]** another object of this invention is to provide a method for forming a plurality of minute sensor electrode dots by said new method for preparing a molecule recognizing film, and for accurately applying a great number of biological samples to be evaluated onto said plural minute sensor electrode dots in a short time and efficiently.

The paragraph beginning at page 4, line 11 has been amended as follows:

[BRIEF DESCRIPTION OF THE INVENTION] SUMMARY

According to one aspect of this invention, with a sensor device comprising organic thin films formed on an arbitrarily chosen electrode board circuit and electrodes, and a transducing element to transduce information obtained by the organic thin films into electric signals, provided is a method for producing the sensor device wherein a solution of a material of the thin film is accurately printed via an ink-jet nozzle as micro-dots onto the required surface of microelectrodes so that the organic thin films are formed on the electrodes, thereby realizing highly dense microelectrodes.

The paragraph beginning at page 4, line 21 has been amended as follows:

According to another aspect of this invention, provided is the sensor device as described in claim 1 wherein the solution of a material of the thin film comprises an electro-conductive polymer dissolved in a solvent.

The paragraph beginning at page 4, line 24 has been amended as follows:

According to another aspect of this invention, provided is the sensor device as described in claim 1 wherein the solution of a material of the thin film as described in claim 1 comprises a solution of a silicone-based surface modifying agent, or a mixture thereof with a solvent.

The paragraph beginning at page 5, line 1 has been amended as follows:

According to another aspect of this invention, provided is the sensor device as described in claim 1 wherein the solution of a material of the thin film as described in claim 1 comprises a mixture resulting from dissolution of a thiol compound in a solvent, and gold thin films are formed on the surface of the electrodes.

The paragraph beginning at page 5, line 6 has been amended as follows:

According to another aspect of this invention, with said sensor device, provided is a method for evaluating a trace amount of liquid wherein a solution of a sample substance to be sensed is ejected into air as micro-dots via an ink-jet nozzle to fall on the surface of organic thin films of microelectrodes so that the substance is submitted to evaluation.

The paragraph beginning at page 5, line 11 has been amended as follows:

According to another aspect of this invention, with said sensor device, provided is a method for evaluating a trace amount of liquid wherein the solution or liquid substance to be sensed and ejected into air as micro-dots via the ink-jet nozzle as described in claim 5 comprises a protein, DNA, antibody, receptor, lectin, a bio-molecule from an animal or plant cell, or a physiologically active substance, or an aqueous solution thereof.

The paragraph beginning at page 5, line 18 has been amended as follows:

According to another aspect of this invention, provided are the sensor device and the method for evaluating the function of a liquid wherein the electrode or electric circuit is formed on a plastic substrate[.].

The paragraph beginning at page 5, line 21 has been amended as follows:

According to another aspect of this invention, provided are the sensor device and the method for evaluating the function of a liquid based on the use of the sensor device wherein the electric circuit is composed of poly-silicon thin film transistors[.].

The paragraph beginning at page 6, line 1 has been amended as follows:

[Fig. 1 gives a diagram to illustrate] Fig. 1 illustrates how minute electro-conductive polymer electrodes are formed by the method of this invention based on the use of an ink-jet.

The paragraph beginning at page 6, line 4 has been amended as follows:

[Fig. 2 gives a diagram to illustrate] Fig. 2 illustrates how a functional solution sample is analyzed **[by the method of this invention]** based on the use of an ink-jet.

The paragraph beginning at page 6, line 7 has been amended as follows:

[Fig. 3 gives a diagram to illustrate] Fig. 3 illustrates how a plurality of functional solution samples are analyzed in a short period on electro-conductive polymer electrodes **[by the method of this invention]** based on the use of an ink-jet.

The paragraph beginning at page 6, line 11 has been amended as follows:

[Fig. 4 is a block diagram to illustrate] Fig. 4 illustrates the principle underlying the assay method of the microsensor device **[of this invention]**.

The paragraph beginning at page 6, line 13 has been amended as follows:

[Fig. 5 gives] Fig. 5 shows an electronic circuit to collect data for analysis using a microsensor device **[of this invention]**.

The paragraph beginning at page 6, line 15 has been amended as follows:

[Fig. 6 gives] Fig. 6 shows an electronic circuit to collect data for analysis using another microsensor device of this invention.

The paragraph beginning at page 6, line 17 has been amended as follows:

[Fig. 7 is a diagram to illustrate] Fig. 7 illustrates how sensor thin membranes having various detection activities are formed on the microelectrodes of a microsensor device **[of this invention]**.

The paragraph beginning at page 6, line 22 has been amended as follows:

[The smallest embodiment necessary for representing] One embodiment of the present invention will be described below with reference to attached figures.

The paragraph beginning at page 6, line 24 has been amended as follows:

Figs. 1, 2, 3, 4, 5 and 6 **[give]** show parts of interest to illustrate the structure of a sensor device embodying the present invention. Fig.1 gives a schematic view of an ink-jet head: 10 stands for an inkjet head; 11 for a head nozzle for ejecting ink droplets; 12 for an electro-conductive polymer applied on the surface of an electrode; 13 for TFT microelectrodes; and 14 for suspended ink droplets ejected via the ink-jet nozzle. The ink-jet head is driven by a piezo-electric element, activating mode, whereby, when an electric signal is delivered from a driving circuit to the piezo-electric element, the piezo-electric element is deformed; a liquid within is pushed out by the deforming pressure; and the liquid is ejected via the nozzle.

The paragraph beginning at page 10, line 9 has been amended as follows:

Then, the assay dependent on the use of a sensor device array produced in the manner as described above will be described. Fig. 4 gives a simple block diagram of a circuit responsible for the assay dependent on the use of a resistor sensor array. Principal functions depicted in the figure are roughly presented by a resistor sensor multiplex section, signal processing circuit section and pattern recognizing section. Namely, the function depicted in this figure **[consists of]** includes picking up signal from a single channel out of the multi-channel resistors, and processing and recognizing it. Accordingly, it is firstly important to accurately detect a change in impedance.

The paragraph beginning at page 10, line 20 has been amended as follows:

The simplest and most accurate way of determining a resistance includes various bridge methods, but these methods are not suitable for measuring a change in resistance. An alternative method includes a resistance to frequency conversion. This method, however, is disadvantageous in that it is accompanied by **[noises]** noise, and requires a rather longtime for measurement. As one general method for detecting a change in resistance, a circuit working on a voltage mode as shown in Fig. 5 has been known. In this circuit, a specific type of resistance sensor is chosen; a constant current is **[flowed through]** applied to it; and the voltage across the sensor is monitored. Then, as the voltage varies in proportion to the resistance, it is possible to detect a change in resistance by following a change in voltage. To determine changes in resistance it is advisable to subtract the voltage given as a base to the sensor by means of a differential amplifier, and then to amplify the differential signal with a high-gain amplifier. The sensitivity of the circuit depicted in Fig. 5 is proportional to the gain of amplifier, and is given by the following equation:

$$V_o = A (I_s R_s - V_{off}),$$

$$\text{where } (\delta V_o / \delta R_s) = A I_s.$$

The paragraph beginning at page 11, line 11 has been amended as follows:

An alternative method by which to detect a change in resistance includes a method working on a current mode. Fig. 6 gives a circuit diagram of the method. In this figure, a constant voltage is applied to a resistor sensor chosen for this purpose. To measure a change in resistance, a constant current supplied from a source is **[flowed through]** applied to the sensor as an offset current; differences in current are removed as a signal; and the signal is amplified. The sensitivity of the circuit is proportional to the current gain of amplifier and to the resistance of sensor.

$$I_0 = A(I_{off} - V_s / R_s)$$

where

$$(\delta I_0 / \delta R_s) = A_s / R_s^2 = A I_s / R_s$$

This type of current detection method commands a higher degree of freedom than does the voltage detection method, and thus simplifies the subsequent processing of signals.

The paragraph beginning at page 11, line 26 has been amended as follows:

The above-described **[Above-described]** semiconductor circuits are usually constituted of field effect transistors (FET) arranged on a monocrystal silicon substrate. However, because in recent years the function of thin film transistors (TFT) formed on a polycrystal silicon (P-Si) film has made a notable progress, it becomes possible to prepare this type of circuit using polycrystal Si thin film transistors (P-Si TFT). The P-Si TFT has advanced so much that its function is essentially equal to that of monocrystal FET. Further, introduction of the method enabling the manufacture of polysilicon at a low temperature allows the use of a spacious glass substrate. This brings about a great cost-reduction and a method that is suitable for the production of sensor devices like the one **[of this invention]** described herein.

The paragraph beginning at page 13, line 3 has been amended as follows:

Several sensor arrays **[consisting]** formed of field effect TFTs could be used for **[thesimultaneous]** the simultaneous identification, classification and quantification of odours or other molecules. These sensors could be used in conjunction with other sensors to detect chemicals. The TFT sensors could be integrated onto a single device. Different electro-conductive polymers are placed upon the gates of the TFT sensors using ink-jet technology. In another modification the array of TFTs could be constructed in a pattern to produce a two-dimensional map of the odour response. The output from each TFT would then resemble the output from a pixel of a CCD camera. Different conducting polymers could be deposited onto different regions of the array to produce a device which was specific to a group or class of chemicals, e. g. aromatics. When the

molecules bind to or react with the polymer a two-dimensional map corresponding to the particular odours will appear.

The paragraph beginning at page 14, line 20 has been amended as follows:

Or, it is possible to plate a gold thin film onto the surface of a microelectrode such that a thiol molecule and gold interact with each other to form a self-organizing agglutination, which results in the formation of a functional, monolayer film. The functional group projecting from the surface of thiol monolayer which has been generated as a result of self-assembly on the gold thin film plated on the microelectrode has a function to selectively recognize a specific bio-molecule or a volatile molecule. For example, as the functional group projecting from the thiol molecule, a biotin derivative may be used. A biotin molecule has a strong binding activity towards a specific binding site of avidin or streptavidin, and its binding constant is about 10^{15} . This is practically the same as that encountered in a covalent bond. To this biotin molecule film is transferred, for example, a solution of avidin-ferritin binding protein via an inkjet nozzle. Then, avidin and biotin are selectively adsorbed; and the ferritin protein molecule is stabilized on the electrode. The thus selectively adsorbed molecule causes a change in refractive index of the entire molecular film, and that change is captured as a change in dielectric constant of the adsorbing molecular film. Namely, it is possible to convert the microelectrode into a polarized thin **[film(capacitor)]** film (capacitor), which serves as a sensor.

The paragraph beginning at page 15, line 14 has been amended as follows:

[ADVANTAGE] ADVANTAGES

According to this invention, provided is a method by which, in contrast with conventional ones, a molecule recognizing film is efficiently and in a short period formed on a microsensor in a uniform and high quality manner. Further, according to this invention, provided is a method by which to accurately introduce a vast number of biological samples to be evaluated in a short period and efficiently to plural, minute sensor electrode dots which have been prepared according to said method for the formation of a molecule recognizing film.

In the claims:

Claims 1-10 and 18-26 have been cancelled.

Claim 11 has been amended as follows:

11. A sensor device comprising:

a circuit having electrodes, wherein [on] at least one [some] of [which] the electrodes comprises an organic thin film [films are] formed by printing a solution of a thin film material onto a surface of the electrode [as micro-dots onto surfaces of electrodes]; and

a transducing element capable of transducing information recognized by the organic thin [films] film into electric signals.

In the abstract:

The abstract has been amended as follows:

[The object of this invention is to provide a method by which to form molecule recognizing films on sensor electrodes efficiently, within a short period, uniformly and in a high quality state. Another object of this invention is to provide a method by which to accurately introduce a vast number of biological samples for evaluation to the plural minute sensor electrode dots within a short period and efficiently.]

In order to form organic thin films on electrodes, a solution of a material for the organic thin film is accurately printed via an ink-jet onto the surface of microelectrodes as required, thereby producing a high density array of microelectrodes. Further, a solution of a sample substance or a liquid substance to be sensed is ejected into air via an ink-jet nozzle to fall to the surface of organic thin membranes on the microelectrodes so that the sample [is] can be evaluated.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Hitoshi FUKUSHIMA et al. Art Unit : Unknown
Serial No. : Not assigned yet Examiner : Unknown
Filed : June 1, 2001
Title : MANUFACTURE OF A MICROSENSOR DEVICE AND A METHOD FOR
EVALUATING THE FUNCTION OF A LIQUID BY THE USE THEREOF

Assistant Commissioner for Patents
Washington, D.C. 20231

DRAWING CHANGE REQUEST

Enclosed, in accordance with U.S. Patent and Trademark Office practice, is a proposed drawing amendment to Figure 3, marked in red and in duplicate.

The amendment to Figure 3 is proposed to correct the spelling of "column" to --column--.

The Examiner is respectfully requested to give authorization to make this drawing amendment.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date:

June 1, 2001

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FIG. 3

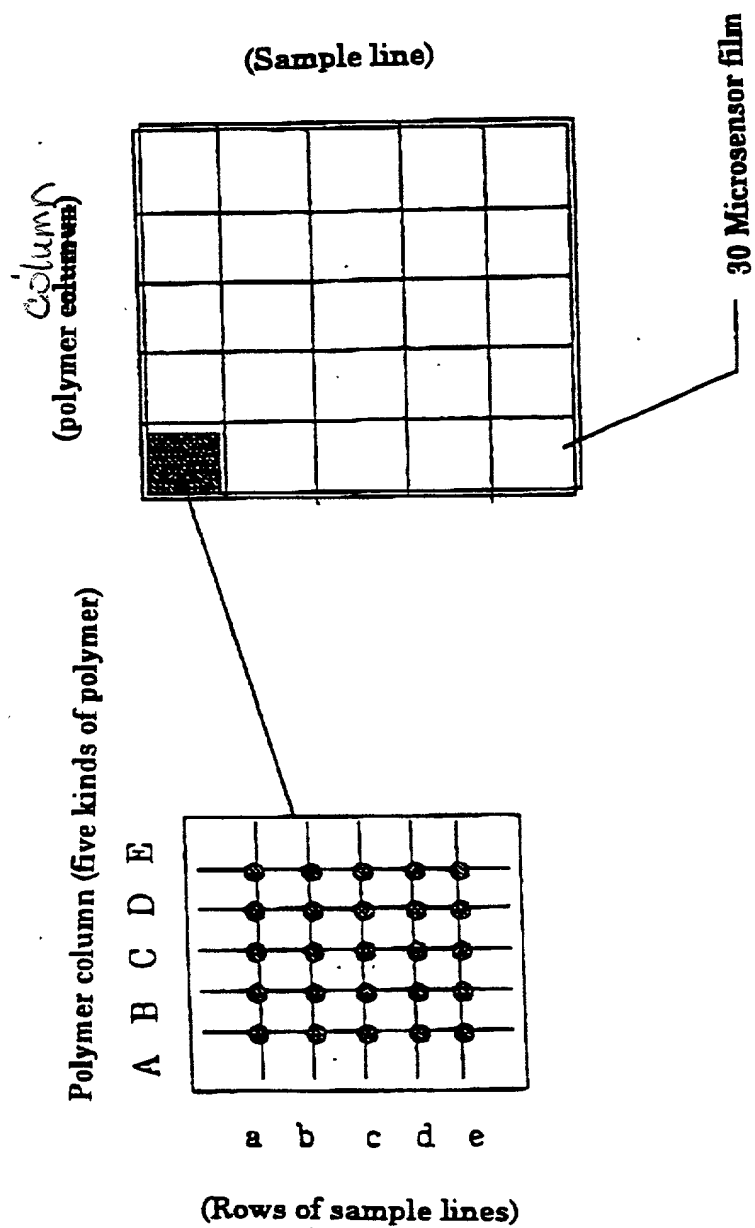


FIG. 3

